REMARKS

Dated: March 16, 2004

Preliminary Matters.

Page 1 of the specification has been amended to state that this application is the National Stage of the PCT application on which priority is claimed.

A revised sequence listing is also submitted herewith to remove duplicate sequences that were inadvertently included in the sequence listing. As originally submitted, SEQ ID NOS: 2, 4, 8, 12, 14, 16, 18 and 20 were identical, as were sequences 1 and 3. The new Sequence Listing eliminates the duplicate sequences. No new matter is added by this amendment.

Page 8 of the specification has been amended to include textual matter that was present in original Figures 3, 4, and 5, which has been removed from the Figures in the replacement Drawing Sheets and to correct the inadvertent duplication of the sequence identification numbers.

Claims 1-11 were subject to a restriction requirement. Applicants elected claims of Group I (claims 1 and 2) directed to peptides that mediate cell permeability. The non-elected Group II claims 3-11 have been cancelled without prejudice.

Claims 1-2 also have been cancelled.

Claims 12-38 have been added. Each of these new claims reads on the subject matter of elected Group I. No new matter is added by these claims.

New Claims 12-38.

New independent claim 12 is directed to an isolated oligopeptide consisting of 12 amino acid residues and having a hydropathy profile in which the side chains of the amino acid residues 2 and 5 have positive hydropathy values, the side chains of amino acid residues 3, 4, 8 and 11 have negative hydropathy values, and the side chains of amino acid residues at positions 1, 6, 7, 9, 10 and 12 can have either positive or negative hydropathy values. Claim 12 further specifies that the oligopeptide be capable of mediating cell permeability to substances that are to be transported into a cell when the oligopeptide is linked to the substance by a covalent or non-covalent linkage. Ample support for this claim can be found in the specification at page 2, line 12 through page 3, line 1 and in the hydropathy profiles of the oligopeptides of the invention shown in Figures 3-5, all of which fit within this description.

Claims 13-20 are directly or indirectly dependent on claim 12.

Claim 13 is directed to a preferred embodiment of the present invention, which is a fusion protein comprising a polypeptide covalently linked to an oligopeptide of claim 12. Support for this claim can be found at page 4, lines 3-4 and page 4, line 30 through page 5, line 3.

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Claim 14 is directly dependent on claim 13 and specifies that the polypeptide is selected from the group consisting of a structural polypeptide, a tumor necrosis factor, an interferon, an interleukin, a lymphokine, a growth factor, and a plasma protein. Support for claim 14 can be found at page 4, lines 5-8.

Claim 15 is directly dependent on claim 13 and specifies that the polypeptide is a cytokine. Support for claim 15 can be found at page 4, line 11.

Claim 16 is directly dependent on claim 13 and specifies that the polypeptide is a costimulatory molecule. Support for claim 16 can be found at page 4, line 12.

Claim 17 is directly dependent on claim 13 and specifies that the polypeptide is a tumor-associated antigen. Support for claim 17 can be found at page 4, line 13.

Claim 18 is directly dependent on claim 13 and specifies that the polypeptide is a peptide fragment of a viral coat. Support for claim 18 can be found at page 4, lines15-18.

Claim 19 is directly dependent on claim 13 and specifies that the polypeptide is a hormone. Support for claim 19 can be found at page 4, lines15-18.

Claim 20 is directly dependent on claim 13 and specifies that the polypeptide is a ribozyme. Support for claim 20 can be found at page 4, lines15-18.

Independent claim 21 is directed to a preferred embodiment of an isolated oligopeptide of the present invention, consisting of 12 amino acid residues and having a hydropathy profile in which the side chains of the amino acid residues 2, 5 and 9 have positive hydropathy values, the side chains of amino acid residues 3, 4, 8 and 11 have negative hydropathy values, and the side chains of amino acid residues at positions 1, 6, 7, 10 and 12 can have either positive or negative hydropathy values. Claim 21 also specifies that the oligopeptide be capable of mediating cell permeability to substances that are to be transported into a cell when the oligopeptide is linked to the substance by a covalent or non-covalent linkage. Ample support for this claim can be found

in the specification at page 2, line 12 through page 3, line 7, and in the hydropathy profiles of the oligopeptides of the invention shown in Figures 3,4, and 5.

Claims 22-39 are directly or indirectly dependent on claim 21.

Claim 22 is directed to a fusion protein comprising a polypeptide covalently linked to an oligopeptide of claim 21. Support for this claim can be found at page 4, lines 3-4 and page 4, line 30 through page 5, line 3.

Claim 23 is directly dependent on claim 22 and specifies that the polypeptide is selected from the group consisting of a structural polypeptide, a tumor necrosis factor, an interferon, an interleukin, a lymphokine, a growth factor, and a plasma protein. Support for claim 23 can be found at page 4, lines 5-8.

Claim 24 is directly dependent on claim 22 and specifies that the polypeptide is a cytokine. Support for claim 24 can be found at page 4, line 11.

Claim 25 is directly dependent on claim 22 and specifies that the polypeptide is a costimulatory molecule. Support for claim 25 can be found at page 4, line 12.

Claim 26 is directly dependent on claim 22 and specifies that the polypeptide is a tumor-associated antigen. Support for claim 26 can be found at page 4, line 13.

Claim 27 is directly dependent on claim 22 and specifies that the polypeptide is a peptide fragment of a viral coat. Support for claim 27 can be found at page 4, lines15-18.

Claim 28 is directly dependent on claim 22 and specifies that the polypeptide is a hormone. Support for claim 28 can be found at page 4, lines15-18.

Claim 29 is directly dependent on claim 22 and specifies that the polypeptide is a ribozyme. Support for claim 29 can be found at page 4, lines15-18.

Independent claim 30 is directed to the oligopeptides set forth in Figures 3-5 and is also supported by the description at page 2, line 12 through page 3, line 1.

Claims 31-38 are directly or indirectly dependent on claim 30.

Claim 31 is directed to a fusion protein comprising a polypeptide covalently linked to an oligopeptide of claim 30 Support for this claim can be found at page 4, lines 3-4 and page 4, line 30 through page 5, line 3.

Claim 32 is directly dependent on claim 31 and specifies that the polypeptide is selected from the group consisting of a structural polypeptide, a tumor necrosis factor, an interferon, an interleukin, a lymphokine, a growth factor, and a plasma protein. Support for claim 32 can be found at page 4, lines 5-8.

Claim 33 is directly dependent on claim 31 and specifies that the polypeptide is a cytokine. Support for claim 33 can be found at page 4, line 11.

Claim 34 is directly dependent on claim 31 and specifies that the polypeptide is a costimulatory molecule. Support for claim 34 can be found at page 4, line 12.

Claim 35 is directly dependent on claim 31 and specifies that the polypeptide is a tumor-associated antigen. Support for claim 35 can be found at page 4, line 13.

Claim 36 is directly dependent on claim 31 and specifies that the polypeptide is a peptide fragment of a viral coat. Support for claim 36 can be found at page 4, lines15-18.

Claim 37 is directly dependent on claim 31 and specifies that the polypeptide is a hormone. Support for claim 37 can be found at page 4, lines15-18.

Claim 38 is directly dependent on claim 31 and specifies that the polypeptide is a ribozyme. Support for claim 38 can be found at page 4, lines15-18.

Each of claims 12-38 is fully supported by the specification. No new matter is added. Claims 12-38 are Patentable.

The present invention, as exemplified by claim 12, is directed to oligopeptides consisting of 12 amino acid residues having cell permeation enhancing properties, which when linked to a substrate, such as a polypeptide, can aid in the transport of the substrate into a cell. Independent claims 21 and 30 are each directed to preferred embodiments of the oligopeptides of the invention. The prior art does not teach or suggest isolated oligopeptides as defined by claims 12, 21 and 30. The prior art does not teach or suggest that an oligopeptide defined by a hydropathy profile as recited in claim 12 or claim 21 will have cell permeability enhancing properties. Nor does the prior art teach or suggest the specific cell permeation mediating oligopeptides set forth in claim 30.

Each of claims 12, 21 and 30 and the claims depending therefrom, are clear and definite and are described in the specification. Hydropathy values for the amino acid side chains are well

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known in the art. One of ordinary skill in the art can readily determine whether a given peptide falls within the scope of claims 12 and 21 by examining the amino acid sequence of the oligopeptide, noting the hydropathy values for the side chains, and evaluating the cell permeability properties as described in the specification in Example 1. Claim 30 is clear and definite on its face. Dependent claims 13-20, 22-29, and 31-38 are each directed to fusion proteins comprising an oligopeptide of claims 12, 21, and 30, respectively, covalently linked to a polypeptide. Fusion proteins are described in the specification at page 4, line 30 through page 5, line 3. The specific polypeptides set forth in claims 14-20, 23-29, and 32-38 are described in the specification and represent known classes of biologically active polypeptides.

Claims 12, 21 and 30 and the claims dependent therefrom are clearly enabled by the teachings of the specification. One of ordinary skill in the art of protein chemistry, at the time the invention was made, could easily select amino acids having the required hydropathy values and construct an oligopeptide within the scope of claims 12 and 21 and the claims dependent therefrom. Claim 30 consists of specific polypeptides described in the drawings. The uses of the polypeptides of the invention are described throughout the specification, particularly on pages 2-5. Example 2 describes the preparation of oligopeptides of the invention and of fusion proteins thereof. The present inventors, by recognizing the importance of the hydropathy profile, provide novel and non-obvious cell permeation mediating oligopeptides.

Each of the newly added claims 12-38 meet all of the requirements of 35 USC §112. Applicants are not aware of any art that teaches or suggests the claimed oligopeptides and fusion proteins.

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Applicants request that the revised Sequence Listing and Replacement Drawing Sheets be entered in the application. Reconsideration and early allowance of claims 12-38 is earnestly solicited.

Respectfully submitted,

Dated: Mas

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CERTIFICATE OF MAILING

I hereby certify that this correspondence, fees and attached replacement drawing sheets referred to therein are being deposited with the United States Postal Service as first class mail with sufficient postage in an envelope addressed to: Commissioner for Patents, P. O. Box 1450, Alexandria, Virginia 22313-1450, on March 16, 2004.

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